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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/566,321	08/04/2006	Rina Aharoni	2819.001	8281

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EXAMINER	
ROBINSON, HOPE A	

ART UNIT	PAPER NUMBER
1652	

MAIL DATE	DELIVERY MODE
08/28/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/566,321	AHARONI ET AL.	
	Examiner	Art Unit	
	HOPE A. ROBINSON	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *5/27/09*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-22,36 and 39-41* is/are pending in the application.

4a) Of the above claim(s) *3,11-17 and 19-22* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-2, 4-10, 18 and 39-41* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *26 January 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Application Status

1. Applicant's response to the Office Action mailed on January 27, 2009 on May 27, 2009 is acknowledged.

Claim Disposition

2. Claims 1-22, 36 and 39-41 are pending. Claims 1-2, 4-10, 18 and 39-41 are under examination based on the species election made. Claims 3, 11-17 and 19-22 are withdrawn from further consideration pursuant to 37 CFR 1.12(b), as being drawn to a non-elected invention, there being no allowable generic or linking claim.

Claim Objection

3. Claims 1 and 5 are objected to because of the following informalities:

For clarity and precision of claim language claim 1 should recite,

"A method of treating or preventing graft rejection in a subject in need thereof, comprising administering a therapeutically effective amount of a copolymer-1 [least one] copolymer1 or copolymer 1-related] heteropolymer in combination with at least one immunosuppressive drug, wherein said copolymer-1 [copolymer 1 or copolymer 1-related] heteropolymer

comprises[ing] one amino acid selected from each of at least three of the following groups:

(a) lysine and arginine;

(b) glutamic acid and aspartic acid;

(c) alanine, glycine and valine; or

(d) tyrosine, tryptophan and phenylalanine".

For clarity, should claim 5 recite "cyclosporine A" or "cyclosporin A".

Correction is required.

Claim Rejections - 35 USC э 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1-2, 4-10, 18 and 39-4 are rejected under 35 U.S.C. 112, first paragraph, because the specification is not enabled for the full scope of the claims.
The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims. The enablement requirement refers to the requirement that the

specification describe how to make and how to use the invention. There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is undue. These factors include, but are not limited to: Quantity of Experimentation Necessary; Amount of direction or guidance presented; Presence or absence of working examples; Nature of the Invention; State of the prior art and Relative skill of those in the art; Predictability or unpredictability of the art and Breadth of the claims (see *In re Wands, 858 F.2d at 737, 8 USPQ2d at1404 (Fed. Cir. 1988)*. The factors most relevant to the instant invention are discussed below.

The claimed invention is directed to a method of treating or preventing graft rejection in a subject in need thereof, comprising administering a therapeutically effective amount of at least one copolymer-1 or coplymer-1-realted heteropolymer in combination with at least one immunosuppressive drug, said copolymer-1 or copolymer-1-related heteropolymer comprising one amino acid selected from each of at least three of the following groups: (a) lysine and arginine; (b)glutamic acid and aspartic acid; (c) alanine, glycine and valine; or tyrosine, tryptophan and phenylalanine (see claim 1 for example). The claimed invention encompasses any structure deemed to be "related" to a copolymer-1. In addition, the claimed invention is directed to a copolymer-1 that is a random heteropolymer, or an ordered heteropolymer or any ordered peptide. The claimed invention encompasses a genus of structures for which no correlation is made between structure and function. The claimed invention is broadly drawn to any antiproliferative drugs, any lymphocyte inhibitors, any antibodies, and any

immunomodulators, steroids and purine antimetabolites which are not supported by the instant specification. The amount of experimentation required to practice the claimed invention is undue based on breath of the claims. The instant specification does not demonstrate or provide guidance as to what protein structure is "an ordered peptide" that falls within the scope of the claimed invention. The instant specification discloses immunosuppressive drugs such as "cyclosporin A, FK 506, rapamycin" etc., however, claim 4 for example recites "steroids, antiproliferative drugs", etc. which is not commensurate in scope. Undue experimentation would be required to practice the full scope of the claims based on the breath of the claims.

The invention is directed to a method of treating or preventing graft rejection in a subject by administering a copolymer-1 (which can be any ordered peptide or a copolymer-1-related heteropolymer) and at least one immunosuppressive drug (which can be any steriod, any antiproliferative drug, any lymphocyte inhibitor, any antibody, etc.). The claimed invention is unpredictability based on the breath of the claims and the lack of guidance in the instant specification. A skilled artisan would have to engage in undue experimentation to examine for example each antibody to see if once administered with any structure, could be deemed as "related to a copolymer-1" would produce the effect of treating or preventing graft rejection.

The specification lacks adequate guidance/direction to enable a skilled artisan to practice the claimed invention commensurate in scope with the claims. The working examples provided do not rectify the missing information in the instant specification

pertaining to the claimed method. The nature and properties of this claim is difficult to ascertain from the examples provided as one of skill in the art would have to engage in undue experimentation to manipulate all the unknown variables and test the method to see if it works as prescribed.

The specification does not provide support for the broad scope of the claims. The issue in this case is the breath of the claims in light of the predictability of the art as determined by the number of working examples, the skill level artisan and the guidance presented in the instant specification and the prior art of record. This make and test position is inconsistent with the decisions of *In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970)* where it is stated that "...scope of claims must bear a reasonable correlation to scope of enablement provided by the specification to persons of ordinary skill in the art...". Without sufficient guidance, determination of having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily and improperly extensive and undue. See *In re Wands, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988)*.

Thus, for all these reasons, the specification is not considered to be enabling for one skilled in the art to make and use the claimed invention as the amount of experimentation required is undue, due to the broad scope of the claims, the lack of guidance and working examples provided in the specification and the high degree of unpredictability. Therefore, applicants have not provided sufficient guidance to enable one of skill in the art to make and use the claimed invention in a manner that reasonably correlates with the scope of the claims, to be considered enabling.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

5. Claims 1-2, 4-10, 18 and 39-41 are rejected under 35 U.S.C. 112, second paragraph, as failing to set forth the subject matter, which applicant (s) regard as their invention.

Claims 1-2, 4-10, 18 and 39-41 are indefinite for the recitation of "a copolymer-1-related heteropolymer" because it is unclear how much relatedness is needed. Are the structures, 10% or 50% identical etc.

Claim 7 lacks clear antecedent basis for "said therapeutically effective amounts".

Claim 8 lacks clarity as the claim more properly depends from claim 1 and instead of claim 2 (see also claim 18).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

6. Claims 1-2, 4-10, 18 and 39-41 are rejected under 35 U.S.C. 102(b) as being anticipated by Aharoni et al. (U.S. Patent No. 5,858,964, January 12, 1999, cited on the IDS filed on September 18, 2006).

Aharoni et al. teach a method for prevention or treatment of graft versus host disease in patients in the course of bone marrow and organ transplantation using a random copolymer consisting of (Ala, Tyr, Glu and Lys) with an average molecular weight of 4,000 to 12,000 which falls within the recited range in the instant claims (see abstract and column 2 of the patent). Aharoni et al. also teach that the copolymer can be optionally used together with other immunosuppressive agents (see column 3 of the patent). Aharoni et al. further teach that other immunosuppressive agents such as cyclosporine (cyclosporine A), methotrexate and prednisone, may be administered with the GLAT copolymer (column 4). Aharoni et al. demonstrate the administration of other immunosuppressive agents together or sequentially with a copolymer (see Example 4 of the patent). Therefore, the limitations of the claims are met by the reference.

7. Claims 1-2, 4-10, 18 and 39-41 are rejected under 35 U.S.C. 102(e) as being anticipated by anticipated by Aharoni et al. (U.S. Patent No. 7,053,043, July 23, 1999).

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art

under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

Aharoni et al. teach methods for treating and preventing host versus graft disease and graft versus host disease comprising random copolymers of amino acids comprising at least one amino acids from the following groups (a) lysine and arginine, (b) glutamic acid and aspartic acid, (c) alanine and glycine and (d) tyrosine and tryptophan (see column 2). Aharoni et al. also teach a molecular weight of 4,000 to 12,000 which falls within the recited range in the instant claims (see abstract and column 2 of the patent). Aharoni et al. teach that "in a preferred embodiment, the random copolymer is used according to the invention for prevention of GVHD and/or HVGD in allogeneic bone marrow transplantation, optionally together with other immunosuppressive agents (see column 5 of the patent) such as cyclosporin A or FK506. Therefore, the limitations of the claims are met by the references.

Basis For NonStatutory Double Patenting

8. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11

F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

9. Claims 1-2, 6, 8-10 and 18 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-18 of US Patent No. 7,053,043. An obvious-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim is not patentably distinct from the reference claim(s) because the examined claim is either anticipated by, or would have been obvious over, the reference claim(s). *See In re Berg, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); In re Goodman, 11F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); and In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985).* Although the conflicting claims are not identical, they are not patentably distinct from each other.

The instant application claim is directed to "a method of treating or preventing graft rejection in a subject in need thereof, comprising administering a therapeutically effective amount of at least one copolymer 1 or copolymer 1-related heteropolymer in combination with at least one immunosuppressive drug, said copolymer 1 or copolymer 1-related heteropolymer comprising one amino acid selected from each of at least three of the following groups: (a) lysine and arginine; (b) glutamic acid and aspartic acid; (c) alanine and glycine; (d) tyrosine, tryptophan and phenylalanine".

The patented claims are directed to "a method for treating or suppressing host-versus-graft disease (HVGD) in a mammalian transplant recipient, comprising administering a therapeutically effective amount of an active ingredient that is a random copolymer consisting of amino acid residues selected from the group consisting of one amino acid from at least three of the following groups, the groups consisting of: (a) lysine and arginine; (b) glutamic acid and aspartic acid; (c) alanine and glycine; (d) tyrosine and tryptophan".

The two sets of claims differ as the instant claims recite "administration with an immunosuppressive drug. However, the patented disclosure indicates that an immunosuppressive drug may be administered with the copolymer 1 (see column 5), thus said combination is contemplated in the patented invention. It is also noted that the instant claims recite, "graft rejection" and the patented claims recite "HVGD" which simply means the recipient's body is rejecting the donor graft as foreign. Thus, the patented claims can be construed as a species in the genus of the instant claims. All other limitations recited in the instant claims can be found within the patented claims.

Although the scope of the claims herein differs, the two sets of claims are directed to similar inventions as the claim language has the similar material. One of ordinary skill in the art would be motivated to modify the instant claims to recite, for example the species that is contained in the patent because the instant application disclosure provides the same information, and said embodiments would clarify the claim by providing the specific species. Therefore, the instant claims are a genus over the patented species. Thus, the patented claims are an obvious variation of the instant application claim, therefore *prima facie* obvious.

10. Claims 1-2, 6, 8-10 and 18 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-16 of US Patent No. 5,858,964. An obvious-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim is not patentably distinct from the reference claim(s) because the examined claim is either anticipated by, or would have been obvious over, the reference claim(s). *See In re Berg, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); In re Goodman, 11F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); and In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985).* Although the conflicting claims are not identical, they are not patentably distinct from each other.

The instant application claim is directed to "a method of treating or preventing graft rejection in a subject in need thereof, comprising administering a therapeutically effective amount of at least one copolymer 1 or copolymer 1-related heteropolymer in

combination with at least one immunosuppressive drug, said copolymer 1 or copolymer 1-related heteropolymer comprising one amino acid selected from each of at least three of the following groups: (a) lysine and arginine; (b) glutamic acid and aspartic acid; (c) alanine and glycine; (d) tyrosine, tryptophan and phenylalanine".

The patented claims are directed to "a method for preventing or treating graft-versus-host disease (GVHD) in a patient about to undergo bone marrow or organ transplantation or suffering from GVHD caused by bone marrow or organ transplantation, which comprises administering to said patient an effective amount of a synthetic random copolymer of average molecular weight 4,000-12,000, herein referred to as GLAT copolymer, said GLAT copolymer consisting of glutamic acid (Glu), lysine (Lys), alanine (Ala) and tyrosine (Tyr) residues in a relative molar ratio of 1.4-2.1 parts of Glu to 3.2-4.2 parts of Lys to 4.0-6.0 parts of Ala to 1.0 part of Tyr".

The two sets of claims differ as the instant claims recite "administration with an immunosuppressive drug. However, the patented disclosure indicates that an immunosuppressive drug may be administered with the copolymer 1 (see column 3), thus said combination is contemplated in the patented invention. It is also noted that the instant claims recite, "graft rejection" and the patented claims recite "GVHD" which simply means the donor's graft is rejecting the recipient as foreign. Thus, the patented claims can be construed as a species in the genus of the instant claims. The patented claims recite other limitations such as the molecular weight which can be found in dependent claims of the instant application. Further, the dependent claims in the patent and instant application recite similar limitations.

Although the scope of the claims herein differs, the two sets of claims are directed to similar inventions as the claim language has the similar material. One of ordinary skill in the art would be motivated to modify the instant claims to recite, for example the species that is contained in the patent because the instant application disclosure provides the same information, and said embodiments would clarify the claim by providing the specific species. Therefore, the instant claims are a genus over the patented species. Thus, the patented claims are an obvious variation of the instant application claim, therefore *prima facie* obvious.

Response to Arguments

11. Applicant's comments filed have been considered in full. Note that the rejections of record are withdrawn, thus applicant's comments are moot and will not be discussed herein. Note also that new grounds of rejection have been instituted under 35 USC 112, first and second paragraph and 102; and Obvious-type double patenting for the reasons stated above.

Conclusion

12. No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Hope A. Robinson whose telephone number is 571-272-0957. The examiner can normally be reached on Monday-Friday from 10:00 a.m. to 6:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang, can be reached at (571) 272-0811.

The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Hope A. Robinson/

Primary Examiner, Art Unit 1652